analysis to be carried out in each of a plurality of separation units using the single reservoir unit; and

an external power unit operatively connected to the reservoir unit for driving the liquid from each reservoir into and through the microchannel of each separation unit.

29. The modular microchannel apparatus system of claim 28, wherein each of two separation units of the plurality has a microchannel of a different length.

30. The modular microchannel apparatus system of claim 28, wherein each of two separation units of the plurality has a microchannel of a different size.--

REMARKS

INTRODUCTORY COMMENTS:

Claims 1-12, 25 and 26 of this Continued Prosecution Application were examined in the Office Action under reply, and stand rejected as follows:

(1) under 35 U.S.C. §112, first paragraph, as drawn to subject matter which was not described in the specification in such a way as to reasonably convey that the inventor(s) has possession of the claimed invention at the time of filing (claims 1-12, 25 and 26);

(2) under 35 U.S.C. §112, second paragraph, as indefinite (claims 1-12, 25 and 26);

(3) under 35 U.S.C. §102(b) as anticipated by U.S. Patent No. 4,806,316 to Johnson et al. (claims 1, 3 and 4);

(4) under 35 U.S.C. §102(e) as anticipated by U.S. Patent No. 6,103,199 to Bjornson et al. (claims 1, 3 and 4);

(5) under 35 U.S.C. §103(a) as obvious over U.S. Patent No. 5,571,410 to Swedberg et al. in view of U.S. Patent No. 4,654,127 to Baker et al. (claims 1-4, 6, 7 and 25);

(6) under 35 U.S.C. §103(a) as obvious over Swedberg et al. in view of Baker et al. and U.S. Patent No. 5,968,331 to Kambara et al. (claims 5, 8, 9 and); and

(7) under 35 U.S.C. §103(a) as obvious over Swedberg et al. in view of Baker et al., Kambara et al., and U.S. Patent No. 5,641,440 to Kaltenbach et al. (claims 10-12).

The rejections are addressed in part by the above amendments to the claims and are otherwise traversed for reasons that will be discussed in detail below.

THE ABOVE AMENDMENTS:

Claims 1 and 25 have been amended and claims 28-30 have been added to clarify the modular nature of the invention. That is, rather than reciting to an ordinary apparatus for separation comprising a separation unit and a reservoir unit, the claims are is directed to a **modular** apparatus for analyte analysis that allows a reservoir unit to be used with each of a plurality of separation units in succession, thereby providing greater flexibility in carrying out separation processes. Claims 1 and 25 have been amended to clarify that at least two separation units are included, each separation unit having a microchannel that enables chemical analysis to be carrier out therein. These separation units are capable of operatively and modularly coupling to the same reservoir unit in succession. Similarly, new claim 28 recites a modular microchannel apparatus system for analyte analysis that includes a reservoir unit for successive operative and modular coupling to any of a plurality of separation units. The separation units may be each substituted with another for operative and modular coupling with the reservoir unit. In short, all claims have been amended to include at least one additional separation unit having a microchannel, thus emphasizing the modular nature of the invention. Once a separation unit is coupled with the reservoir unit, an external power unit delivers liquid from the reservoir into and through the microchannel of the separation unit.

Support for these amendments can be found throughout the application as filed. For example, it is disclosed on page 3, line 19 to page 4, line 2 that a wide variety of different parts can be made such that a skilled person can pick and choose among them for the particular application of use. It is also disclosed that the separation units, each with a microchannel of a different length, can be used with the same reservoir unit. In addition, as described on page 5, line 22 to page 6, line 7, the modular nature of this apparatus allows for substitution of components to accommodate the specific needs associated with analyzing a particular sample. Furthermore, external power units are described on page 12, lines 2 to 10. Thus, all pending

claims are fully supported by the original disclosure of the application, and no new matter has been added.

THE REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH:

Claims 1 and 25 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter not described in the specification in such a way as to reasonably convey that the inventors had possession of the claimed invention. Specifically, the Examiner has stated that: "[t]here is no mention of the process of supplying liquid reagents and analyte to the separation unit upon application of a driving force resulting from *simultaneous* operative and modular coupling." Thus, it appears that the Examiner has issued this rejection because the term "simultaneous" is absent from the specification.

Applicants disagree with the rejection for the reasons set forth in the Amendment Under 37 CFR §1.116 submitted on December 18, 2000. That is, it is evident that from the figures accompanying the cited text that modular and operative coupling of the reservoir unit to a separation unit may be carried out simultaneously so as to enable application of a driving force to supply liquid reagents and analyte to the separation unit. With the above amendments to clarify the modular nature of the invention, all references to the term "simultaneous" have been deleted from the claims. It should be noted, then, that this clarifying amendment does not exclude simultaneous operative and modular coupling from the scope of the claims to the extent that such simultaneous coupling is supported by the application as filed.

For the foregoing reasons, applicants respectfully request reconsideration and withdrawal of the rejection.

THE REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH:

Claims 1-12, 25 and 26 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter that applicants regard as the invention. Specifically, the Examiner has contended that the term "having dimensions compatible with the separation unit" is indefinite. With the above amendments, applicants have now clarified that the reservoir unit has "dimensions compatible

with each of the separation units **for coupling operatively and modularly to supply liquid reagents and analyte**" to the separation units (emphasis added). Accordingly, reconsideration sand withdrawal of this rejection is respectfully requested as well.

THE 35 U.S.C. §102(B) REJECTION OVER JOHNSON ET AL.:

Claims 1, 3 and 4 were rejected as anticipated by Johnson et al. In issuing this rejection, the Examiner contends that Johnson et al. teaches a separation unit having microchannels in which analyte can be driven to pass through and a prepackaged reservoir unit having a reservoir with dimensions compatible with the separation unit. The Examiner further states that when the separation unit and the reservoir unit are coupled in fixed alignment via threads on the separation unit, simultaneous operative and modular coupling creates a driving force, gravity, to supply liquid reagents to the separation unit. The Examiner refers to column 4, lines 4-57 and FIGS. 1-9 in support of the rejection.

Applicants disagree with the Examiner's contention that Johnson et al. teaches a separation unit having microchannels and a prepackaged reservoir unit having a reservoir with dimensions compatible with the separation unit. Johnson et al. is directed to a disposable self-pipetting device for analysis and not to separation *per se*. There is no disclosure with respect to separation of any type. In fact, the term "separation" is absent from Johnson et al. In addition, there is no disclosure with respect to microchannels. As pointed out by the Examiner, gravity causes the reservoir unit of Johnson et al. to supply liquid reagents to channels in the self-pipetting device. Since microchannels generally exhibit a large surface area to volume ratio, surface and other forces dominate over gravity in effecting fluid flow in microchannels. Thus, the channels described in Johnson et al. are likely channels that exhibit a large cross-sectional area, not microchannels. In short, Johnson disclosed generalized analytical device rather than a microchannel apparatus using separation units.

It is well settled that anticipation requires a showing that all elements of a claimed invention are disclosed in a single prior art reference. *In re Bond*, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). As discussed above, the invention is directed to a **modular microchannel apparatus system** for analyte analysis that is not disclosed in Johnson et al. Not only does the

claimed system allow a separation unit to be modularly and operatively coupled to a reservoir unit, the system includes at least one additional separation unit. That is, the system comprises at least two separation units and a reservoir unit that has dimensions compatible with each of the separation units to allow for operative and modular coupling. Since Johnson et al. provides no disclosure with respect to separation, microchannels or modularity, Johnson et al. cannot anticipate the pending claims. Accordingly, applicants request reconsideration and withdrawal of the rejection over Johnson et al.

THE 35 U.S.C. §102(E) REJECTION OVER BJORNSON ET AL.:

Claims 1, 3 and 4 were also rejected as anticipated by Bjornson et al. In issuing this rejection, the Examiner asserts that Bjornson et al. teaches a separation unit having microchannels in which an analyte can be driven to pass through. The Examiner further states that Bjornson et al. teaches a reservoir unit having one or more reservoirs with dimensions compatible with the separation unit for operative and modular coupling in fixed alignment. In particular, the Examiner points to FIGS. 5-12 as well as column 26, line 15 to column 27, line 38 as support for this rejection. Microfluidic devices employing an array of cavity structures for fluid transfer are generally described in the cited sections and figures.

As stated above, the claimed invention was conceived and reduced to practice before the effective date of Bjornson et al. as evidenced by a Declaration Under 37 C.F.R. §1.131 accompanying these papers. Thus, Bjornson et al. does not represent prior art with respect to the claimed invention. In addition, the pending claims are directed to a **modular microchannel apparatus system** for analyte analysis as emphasized above. There is no disclosure in Bjornson et al. relating to modularity. That is, the apparatus and method described in Bjornson et al. do not include a plurality of separation units each including a microchannel through which an analyte can be driven. There is no mention of separation units that can be substituted with one another, nor does Bjornson et al. disclose a reservoir unit that may be coupled to each of a plurality of separation units. Thus, Bjornson et al. does not anticipate the pending claims, and applicants respectfully request withdrawal of this rejection as well.

- Not in Claim

THE 35 U.S.C. §103(A) REJECTION OVER SWEDBERG ET AL. IN VIEW OF BAKER ET AL.:

Claims 1-4, 6, 7 and 25 are again rejected as obvious over Swedberg et al. in view of Baker et al. The Examiner repeated reasoning from the previous Office Action that it would have been obvious to one skilled in the art at the time of the invention to include prepackaged liquid reagents in the apparatus of Swedberg et al. in order to avoid contaminating the reagents before introduction into the microchannel and to eliminate the need for handling of calibrated reagents. The Examiner also reiterated her position that Baker et al. teaches an apparatus that contains various parts that can be assembled for use without extensive calibration or testing. In addition, the Examiner stated that modular coupling might, as defined by the application, include a rotation step as required by Baker et al.

Applicants again submit that the three basic criteria for *prima facie* obviousness have not been met. As stated before, it appears that the Examiner employed improper hindsight analysis in issuing this rejection because the rejection is based on knowledge that was gleaned from applicants' own disclosure. That is, without a priori knowledge of applicants' disclosure, there is no reason as to why Swedberg et al. should be read with Baker et al. In addition, there would be no reasonable expectation of success that the claimed invention would result if Baker et al. were read together with Swedberg et al. For example, as reflected in its title, Baker et al. is directed to a **single-use** device. All pending claims have now been amended to clarify that the inventive apparatus and system include a plurality of separation units allowing multiple use. There is no reason to provide a reservoir unit that is capable of successive coupling to each of a plurality of separation units if the device were intended for single use. A single-use reservoir unit would lack sufficient quantities of reagents for multiple use with a plurality of separation units.

Furthermore, the claims now recite an element that is not taught or suggested by the combination of the cited references, i.e., **an additional separation unit**. In addition, the reservoir unit has dimensions compatible with **each of the separation units** to allow for operative and modular coupling to the separations unit to supply liquid reagents and analyte thereto. Such operative and modular coupling, as set forth in amended claims 1 and 25, may be carried out in **succession**. Alternatively, as set forth in claim 28, each **separation unit may be substituted with another for coupling to the same reservoir unit**. Such modularity, involving

a plurality of separation units that can each be modularly and operatively coupled to the same reservoir unit, is neither disclosed in or suggested by the cited references.

For the above reasons, reconsideration and withdrawal of the rejection is accordingly respectfully requested.

THE REJECTION UNDER 35 U.S.C. §103(A) OVER SWEDBERG ET AL. IN VIEW OF BAKER ET AL. AND KAMBARA ET AL.:

Claims 5, 8, 9 and 26 have again been rejected as obvious over Swedberg et al. in view of Baker et al. and Kambara et al. as applied to claim 2, the Examiner referring to the previous Office Action. The Examiner previously contended that it is obvious to include the Kambara et al. probes in the in the apparatus of Swedberg et al. and Baker et al. probes to drive liquid into microchannels in order to reduce the time and labor needed for reagent introduction.

As before, applicants respectfully disagree. The rejected claims all depend from independent claim 1 which, as discussed above, is nonobvious over Swedberg et al. and Baker et al. as neither patent discloses or suggest that a reservoir unit that can be coupled to each of a plurality of separation units as discussed above. The addition of Kambara et al. does not provide any further teaching or suggestion to include an **additional separation unit** that can be coupled to the reservoir unit. As disclosed in the abstract of Kambara et al., a single separation component allows for repeated use of the gel capillaries. Thus, Kambara et al. teaches that one separation unit is sufficient and that there is no need for modularity that allows substitution of separation units. Accordingly, this patent effectively teaches away from use of a plurality of separation units that can be modularly and operatively coupled to a single reservoir unit.

As the references in combination fail to disclose each and every element of the claims, withdrawal of the rejection is thus requested.

THE REJECTION UNDER 35 U.S.C. §103(A) OVER SWEDBERG ET AL. IN VIEW OF BAKER ET AL., KAMBARA ET AL. AND KALTENBACH ET AL.:

Claims 10-12 were again rejected as obvious over Swedberg et al. in view of Baker et al., Kambara et al. and Kaltenbach et al., the Examiner citing Swedberg et al., Baker et al. and Kambara et al. as before with reference to the previous Office Action. In the previous rejection,

the Examiner stated that the addition of the peltier plate recited in these claims would have been obvious to one skilled in the art given the teaching of Kaltenbach et al. However, the rejected claims depend from independent claim 1, which is nonobvious over Swedberg et al., Baker et al. and Kambara et al. for the reasons discussed above. The addition of Kaltenbach et al. does not provide any further teaching or suggestion of a reservoir unit that may be coupled to each of a plurality of separation units in succession or of separation units that may be substituted with each other. Thus, no additional basis for the rejection of the independent claim is provided. As the rejected claims all depend from a nonobvious claim, they too are nonobvious. Reconsideration and withdrawal of the rejection is thus requested.

CONCLUSION

For all of the above reasons, it is submitted that the application comports with all requirements of 35 U.S.C. §112, and that the pending claims define an invention that is patentable over the art. As the application should now be in condition for allowance, a prompt indication to that effect would be appreciated. If the Examiner have any questions concerning this communication, she is welcome to contact Michael Beck at (650) 485-3864.

Respectfully submitted,

July 25, 2001
Date

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APPENDIX A

(THE REDACTED CLAIMS INDICATING THE AMENDMENTS MADE)

1. (Four Times Amended) A modular microchannel apparatus for the chemical analysis of an analyte in a sample, comprising:

~~(a) a separation unit having a microchannel, in which the analyte can be driven to pass through the microchannel due to the molecular characteristics thereof and wherein the time for the analyte to pass through the microchannel is indicative of the molecular characteristics of the analyte; and~~

~~(b) a reservoir unit having one or more reservoirs having dimensions compatible with the separation unit operatively and modularly coupled in fixed alignment to the separation unit to supply liquid reagents and analyte thereto upon application of a driving force resulting from simultaneous operative and modular coupling, the reservoirs having prepackaged liquid reagents therein before the reservoir unit is coupled with the separation unit.~~

(a) at least two separation units each including (i) a microchannel through which a sample comprising an analyte may be driven in a determinable time period, said time period indicative of molecular characteristics of the analyte, (ii) an inlet allowing input of liquid into the microchannel, and (iii) an outlet allowing removal of liquid from the microchannel;

(b) a single reservoir unit comprised of a reservoir adapted to contain a liquid for introduction through the inlet and into the microchannel of each separation unit, the reservoir having dimensions that enable successive operative and modular coupling to each separation unit so as to allow transfer of liquid from the reservoir unit into the microchannel of each separation unit, thereby enabling chemical analysis to be carried out in each of a plurality of separation units using the single reservoir unit; and

(c) an external power unit operatively connected to the reservoir unit for driving the liquid from the reservoir into and through the microchannel of each separation unit.

2. (Twice Amended) An apparatus according to claim 1, wherein at least one of the separation units is chip-shaped and formed from a first half and a second half each having a substantially planar surface facing and joining the other half, wherein at least one of the planar surfaces has a channel thereon such the joining of the two surfaces forms the microchannel.

3. (Twice Amended) An apparatus according to claim 1, wherein at least one of the separation units has one or more openings leading to the microchannel capable of admitting liquid reagents such that when the separation unit and the reservoir unit are operatively and modularly coupled, the openings are aligned with the reservoirs thereby allowing the liquid reagents and the analyte to pass from the reservoirs into the microchannel without substantial leakage.

4. (Twice Amended) An apparatus according to claim 2, wherein at least one of the separation units includes a substrate comprised of a material other than silicon or silicon dioxide in which the first microchannel is formed by laser ablation.

5. (Twice Amended) An apparatus according to claim 2, wherein the reservoir unit includes a membrane that covers at least one of the reservoirs confining the prepackaged liquid reagent therein, wherein the membrane is penetrable with a probe for applying a driving force to drive movement of liquid reagent and analyte from the reservoir through the microchannel of at least one of the separation units.

6. (Twice Amended) An apparatus according to claim 2, wherein both substantially planar surfaces of the separation unit having a first half and a second half have a laser-ablated channel thereon and the two channels join to form the microchannel.

7. (Twice Amended) An apparatus according to claim 2, wherein the channel of at least one separation unit is formed by laser ablation.

8. (Twice Amended) An apparatus according to claim 2, ~~further comprising~~ wherein the external power unit comprises a powering plate operatively and modularly coupled to the reservoir unit, the powering plate having an electrical connection to ~~at least one of the reservoirs~~ the reservoir to provide a driving force to drive movement of the liquid reagents and analyte from the reservoir through the microchannel.

10. (Twice Amended) An apparatus according to claim 26, further comprising a peltier plate operatively and modularly coupled to the support plate for controlling the temperature of at least one of the separation units.

11. (Twice Amended) An apparatus according of claim 10, wherein the peltier plate can be used to heat or cool at least one of the separation units by selecting an appropriate mode of operation.

25. (Thrice Amended) A kit for making a modular microchannel apparatus for the chemical analysis of an analyte in a sample, comprising:

~~(a) a separation unit having a microchannel, in which the analyte can be driven to pass through the microchannel due to the molecular characteristics thereof and wherein the time for the analyte to pass through the microchannel is indicative of the molecular characteristics of the analyte; and~~

~~(b) a reservoir unit having one or more reservoirs having dimensions compatible with the separation unit for coupling operatively and modularly to the separation unit in fixed alignment to supply liquid reagents and analyte thereto upon application of a driving force resulting from simultaneous operative and modular coupling, the reservoirs having prepackaged liquid reagents therein.~~

(a) at least two separation units each including (i) a microchannel through which a sample comprising an analyte may be driven in a determinable time period, said time period indicative of molecular characteristics of the analyte, (ii) an inlet allowing input of liquid into the microchannel, and (iii) an outlet allowing removal of liquid from the microchannel;

(b) a single reservoir unit comprised of a reservoir adapted to contain a liquid for introduction through the inlet and into the microchannel of each separation unit, the reservoir having dimensions that enable successive operative and modular coupling to each separation unit so as to allow transfer of liquid from the reservoir unit into the microchannel of each separation unit, thereby enabling chemical analysis to be carried out in each of a plurality of separation units using the single reservoir unit; and

(c) an external power unit operatively connected to the reservoir unit for driving the liquid from the reservoir into and through the microchannel of each separation unit.

26. (Twice Amended) The apparatus according to claim 9, further comprising a support plate for operatively and modularly coupling ~~coupled~~ to the separation units.